PMS2 gene

PMS1 homolog 2, mismatch repair system component

Normal Function

The *PMS2* gene provides instructions for making a protein that plays an essential role in repairing DNA. This protein helps fix mistakes that are made when DNA is copied (DNA replication) in preparation for cell division. The PMS2 protein joins with another protein called MLH1 (produced from the *MLH1* gene) to form a protein complex. This complex coordinates the activities of other proteins that repair mistakes made during DNA replication. Repairs are made by removing the section of DNA that contains mistakes and replacing it with a corrected DNA sequence. The *PMS2* gene is a member of a set of genes known as the mismatch repair (MMR) genes.

Health Conditions Related to Genetic Changes

Lynch syndrome

Mutations in the *PMS2* gene have been reported in about 2 percent of families with Lynch syndrome that have an identified gene mutation. Lynch syndrome increases the risk of many types of cancer, particularly cancers of the colon (large intestine) and rectum, which are collectively referred to as colorectal cancer. People with Lynch syndrome also have an increased risk of cancers of the endometrium (lining of the uterus), ovaries, stomach, small intestine, liver, gallbladder duct, upper urinary tract, and brain. *PMS2* gene mutations involved in this condition lead to the production of an abnormally short or inactive PMS2 protein that cannot efficiently repair mistakes made during DNA replication. The errors accumulate as the cells continue to divide, which may cause the cells to function abnormally, increasing the risk of tumor formation in the colon or another part of the body.

Some mutations in the *PMS2* gene can cause a variant of Lynch syndrome called Turcot syndrome. In addition to colorectal cancer, people with Turcot syndrome tend to develop a particular type of brain tumor called a glioblastoma.

ovarian cancer

other cancers

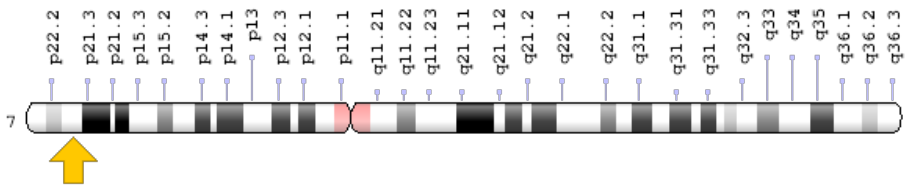
While Lynch syndrome is associated with a mutation in one copy of the *PMS2* gene, very rarely, individuals in affected families inherit two *PMS2* gene mutations, one from each parent. Most often in these cases, the same mutation occurs in both copies of the gene (a homozygous mutation). People with a homozygous *PMS2* gene

mutation have a syndrome distinct from Lynch syndrome. In addition to colorectal cancer, these individuals may develop cancers of the blood (leukemia or lymphoma). Some of these individuals will also develop characteristic features of a condition known as neurofibromatosis, including noncancerous tumors that grow along nerves (neurofibromas) and light brown patches of skin called café-au-lait spots. The onset of colon cancer in these individuals is extremely early, often occurring during childhood. This syndrome involving colon cancer, leukemia or lymphoma, and neurofibromatosis is sometimes called CoLoN.

Chromosomal Location

Cytogenetic Location: 7p22.1, which is the short (p) arm of chromosome 7 at position 22.1

Molecular Location: base pairs 5,970,925 to 6,009,106 on chromosome 7 (Homo sapiens Annotation Release 108, GRCh38.p7) (NCBI)



Credit: Genome Decoration Page/NCBI

Other Names for This Gene

- DNA mismatch repair gene homologue
- HNPCC4
- MLH4
- PMS2-C terminal -like
- PMS2 postmeiotic segregation increased 2 (S. cerevisiae)
- PMS2_HUMAN
- PMS2CL
- PMSL2
- postmeiotic segregation increased (S. cerevisiae) 2

Additional Information & Resources

Educational Resources

- American Medical Association and National Coalition for Health Professional Education in Genetics: Understand the Basics of Genetic Testing for Hereditary Colorectal Cancer
  http://www.nchpeg.org/documents/crc/Basics%20of%20genetic%20testing.pdf
- Cancer Medicine (sixth edition, 2003): DNA Mismatch Repair Gene Defects and HNPCC
  https://www.ncbi.nlm.nih.gov/books/NBK12469/#A1595
- Molecular Biology of the Cell (fourth edition, 2002): Defects in DNA Mismatch Repair Provide an Alternative Route to Colorectal Cancer
  https://www.ncbi.nlm.nih.gov/books/NBK26902/#A4345

GeneReviews

- Lynch Syndrome
  https://www.ncbi.nlm.nih.gov/books/NBK1211

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28PMS2%5BTIAB%5D%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+1800+days%22%5Bdp%5D

OMIM

- MISMATCH REPAIR CANCER SYNDROME
  http://omim.org/entry/276300
- NEUROFIBROMATOSIS, TYPE I
  http://omim.org/entry/162200
- POSTMEIOTIC SEGREGATION INCREASED, S. CEREVISIAE, 2
  http://omim.org/entry/600259

Research Resources

- Atlas of Genetics and Cytogenetics in Oncology and Haematology
  http://atlasgeneticsoncology.org/Genes/GC_PMS2.html
- ClinVar
  https://www.ncbi.nlm.nih.gov/clinvar?term=PMS2%5Bgene%5D
- HGNC Gene Family: MutL homologs
  http://www.genenames.org/cgi-bin/genefamilies/set/1027

- HGNC Gene Symbol Report
  http://www.genenames.org/cgi-bin/gene_symbol_report?q=data/hgnc_data.php&hgnc_id=9122
- NCBI Gene
  https://www.ncbi.nlm.nih.gov/gene/5395
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